AMENDMENTS TO THE CLAIMS

This Listing of Claims will replace all prior versions, including listings, of claims in the application.

Listing of Claims

1 (Original): A tyrosine kinase inhibitor protein consisting of the cap region of a c-Abl protein or a functional equivalent thereof.

2 (Original): A tyrosine kinase inhibitor protein according to claim 1 wherein the c-Abl protein is a mammalian c-Abl protein.

3 (Original): A tyrosine kinase inhibitor protein according to claim 2 wherein the c-Abl protein is human.

4 (Original): A tyrosine kinase inhibitor protein according to claim 3 wherein the c-Abl protein is type 1a c-Abl.

5 (Original): A tyrosine kinase inhibitor protein according to claim 3 wherein the c-Abl protein is type 1b c-Abl.

6 (Original): A tyrosine kinase inhibitor protein according to claim 4 consisting of amino acids 1-61 of type 1a c-Abl.

7 (Original): A tyrosine kinase inhibitor protein according to claim 5 consisting of amino acids 1-80 of Type 1b c-Abl.

8 (Original): A tyrosine kinase inhibitor protein according to claim 2 wherein the c-Abl protein is murine.

9 (Original): A tyrosine kinase inhibitor protein according to claim 8 wherein the c-Abl protein is type I c-Abl.

10 (Original): A tyrosine kinase inhibitor protein according to claim 8 wherein the c-Abl protein is type IV c-Abl.

11 (Original): A tyrosine kinase inhibitor protein according to claim 9 consisting of amino acids 1-63 of type I c-Abl.

12 (Original): A tyrosine kinase inhibitor protein according to claim 10 consisting of amino acids 1-80 of type IV c-Abl.

13 (Currently amended): A tyrosine kinase inhibitor protein or functional equivalent thereof according to ~~any one of claims 1-12~~ claim 1 which inhibits a tyrosine kinase protein containing SH2 and SH3 domains.

14 (Original): A tyrosine kinase inhibitor protein or functional equivalent according to claim 13 which inhibits Abl, Src or Fyn.

15 (Original): A tyrosine kinase inhibitor protein or functional equivalent thereof according to claim 13 which inhibits an oncogenic form of said tyrosine kinase protein containing SH2 and SH3 domains.

16 (Original): A tyrosine kinase inhibitor protein or functional equivalent thereof according to claim 15 which inhibits an oncogenic form of Abl, Src or Fyn.

17 (Original): A tyrosine kinase inhibitor protein or functional equivalent thereof according to claim 16 which inhibits an oncogenic form of Abl.

18 (Original): A tyrosine kinase inhibitor protein or functional equivalent thereof according to claim 17 which inhibits BCR-Abl.

19 (Currently amended): A fusion protein comprising a tyrosine kinase inhibitor protein or a functional equivalent thereof according to ~~any one of claims 1 to 18~~ claim 1 fused to a marker domain.

20 (Original): A fusion protein according to claim 19 wherein the marker domain is green fluorescent protein.

21 (Currently amended): An antibody that which binds to a tyrosine kinase inhibitor protein or a functional equivalent thereof according to ~~any one of claims 1 to 18 or to a fusion protein according to claim 19 or claim 20~~ claim 1.

22 (Currently amended): A nucleic acid molecule encoding a tyrosine kinase inhibitor protein or a functional equivalent thereof according to ~~any one of claims 1-18 or a fusion protein according to claim 19 or 20~~ claim 1.

23 (Original): An antisense nucleic acid molecule which binds under high stringency conditions to a nucleic acid molecule according to claim 22.

24 (Currently amended): A vector comprising a nucleic acid molecule according to claim 22 ~~or claim 23~~.

25 (Currently amended): A host cell transformed or transfected with a nucleic acid molecule according to claim 22 ~~23 or a vector according to claim 24~~.

26 (Currently amended): A method for preparing a tyrosine kinase inhibitor protein or a functional equivalent thereof ~~according to any one of claims 1 to 18 or a fusion protein according to claim 19 or 20~~ comprising culturing a host cell containing a nucleic acid molecule according to claim 22 under conditions whereby said protein is expressed and recovering said protein thus produced.

27 (Original): A method of identifying an activator compounds that inhibits autoinhibition of c-Abl by the cap region comprising contacting c-Abl with a candidate activator compound and assessing whether binding between the cap region of c-Abl and the catalytic and SH2 and/or SH3 domains of c-Abl has been inhibited.

28 (Original): An activator compound identified or identifiable by the method of claim 27.

29 (Original): A method for identifying a modulator compound that restores autoinhibition of c-Abl by the cap region comprising contacting c-Abl and an activator compound according to claim 28 with a candidate modulator compound and assessing whether binding between the cap region of c-Abl and the catalytic and SH2 and/or SH3 domains of c-Abl is restored.

30 (Original): A modulator compound identified or identifiable by the method of claim 29.

31 (Currently amended): A method of modulating the activity of a protein tyrosine kinase comprising providing a cell with an active agent said active agent selected from the group consisting of

(i) a tyrosine kinase inhibitor protein or a functional equivalent thereof according to claim 1;

(ii) a fusion protein comprising said tyrosine kinase inhibitor protein or a functional equivalent thereof fused to a maker domain;

(iii) a nucleic acid molecule encoding said tyrosine kinase inhibitor protein or a functional equivalent thereof;,

(iv) a nucleic acid molecule encoding said fusion protein;

(v) an antisense molecule which binds under high stringency conditions to a nucleic acid molecule of (iii);

(vi) an antisense molecule which binds under high stringency conditions to a nucleic acid molecule of (iv);

(vii) an activator compound that inhibits autoinhibition of c-Abl by the cap region; and

(viii) a modulation compound that restores autoinhibition of c-Abl by the cap region. ~~any one of claims 1-18, a fusion protein according to claim 19 or 20, a nucleic acid molecule according to claim 22, an antisense nucleic acid molecule according to claim 23, an activator compound according to claim 28 or a modulator compound according to claim 30.~~

32 (Original): Use of a cap region of a c-Abl protein or a functional equivalent thereof as a tyrosine kinase inhibitor.

33 (Currently amended): ~~A~~ An active agent for use as a pharmaceutical said active agent selected from the group consisting of:

(i) a tyrosine kinase inhibitor protein or a functional equivalent thereof according to claim 1;

(ii) a fusion protein comprising said tyrosine kinase inhibitor protein or a functional equivalent thereof fused to a maker domain;

(iii) a nucleic acid molecule encoding said tyrosine kinase inhibitor protein or a functional equivalent thereof;

(iv) a nucleic acid molecule encoding said fusion protein;

(v) an antisense molecule which binds under high stringency conditions to a nucleic acid molecule of (iii);

(vi) an antisense molecule which binds under high stringency conditions to a nucleic acid molecule of (iv);

(vii) an activator compound that inhibits autoinhibition of c-Abl by the cap region; and

(viii) a modulation compound that restores autoinhibition of c-Abl by the cap region. ~~any one of claims 1-18, a fusion protein according to claim 19 or 20, a nucleic acid molecule according to claim 22, an antisense nucleic acid molecule according to claim 23, an activator compound according to claim 28 or a modulator compound according to claim 30 for use as a pharmaceutical~~.

34 (Currently amended): A pharmaceutical composition comprising an active agent in conjunction with a pharmaceutically-acceptable carrier molecule, said active agent selected from the group consisting of:

(i) a tyrosine kinase inhibitor protein or a functional equivalent thereof according to claim 1;

(ii) a fusion protein comprising said tyrosine kinase inhibitor protein or a functional equivalent thereof fused to a maker domain;

(iii) a nucleic acid molecule encoding said tyrosine kinase inhibitor protein or a functional equivalent thereof;

(iv) a nucleic acid molecule encoding said fusion protein;

(v) an antisense molecule which binds under high stringency conditions to a nucleic acid molecule of (iii);

(vi) an antisense molecule which binds under high stringency conditions to a nucleic acid molecule of (iv);

(vii) an activator compound that inhibits autoinhibition of c-Abl by the cap region; and

(viii) a modulation compound that restores autoinhibition of c-Abl by the cap region. ~~any one of claims 1-18, a fusion protein according to claim 19 or 20, a nucleic acid molecule according to claim 22, an antisense nucleic acid molecule according to claim 23, an activator compound according to claim 28 or a modulator compound according to claim 30 in conjunction with a pharmaceutically-acceptable carrier molecule~~.

35 (Currently amended): Use of an active agent in the manufacture of a medicament for the treatment of a disease with aberrant tyrosine kinase activity, said agent selected from the group consisting of:

(i) a tyrosine kinase inhibitor protein or a functional equivalent thereof according to claim 1;

(ii) a fusion protein comprising said tyrosine kinase inhibitor protein or a functional equivalent thereof fused to a maker domain;

(iii) a nucleic acid molecule encoding said tyrosine kinase inhibitor protein or a functional equivalent thereof;

(iv) a nucleic acid molecule encoding said fusion protein;

(v) an antisense molecule which binds under high stringency conditions to a nucleic acid molecule of (iii);

(vi) an antisense molecule which binds under high stringency conditions to a nucleic acid molecule of (iv);

(vii) an activator compound that inhibits autoinhibition of c-Abl by the cap region; and

(viii) a modulation compound that restores autoinhibition of c-Abl by the cap region. ~~any one of claims 1-18, a fusion protein according to claim 19 or 20, a nucleic acid molecule according to claim 22, an antisense nucleic acid molecule according to claim 23, an activator compound according to claim 28, a modulator compound according to claim 30, or a pharmaceutical composition according to claim 34 in the manufacture of a medicament for the treatment of a disease associated with aberrant tyrosine kinase activity~~.

36 (Currently amended): A method of treating a disease associated with aberrant tyrosine kinase activity in a patient, comprising administering to the patient an active agent selected from the group consisting of:

(i) a tyrosine kinase inhibitor protein or a functional equivalent thereof according to claim 1;

(ii) a fusion protein comprising said tyrosine kinase inhibitor protein or a functional equivalent thereof fused to a maker domain;

(iii) a nucleic acid molecule encoding said tyrosine kinase inhibitor protein or a functional equivalent thereof;,

(iv) a nucleic acid molecule encoding said fusion protein;

(v) an antisense molecule which binds under high stringency conditions to a nucleic acid molecule of (iii);

(vi) an antisense molecule which binds under high stringency conditions to a nucleic acid molecule of (iv);

(vii) an activator compound that inhibits autoinhibition of c-Abl by the cap region;

(viii) a modulation compound that restores autoinhibition of c-Abl by the cap region; and

(xi) a pharmaceutical composition comprising (ii), (iii), (iv), (v), (vi), (vii) or (viii). ~~tyrosine kinase inhibitor protein or a functional equivalent thereof according to any one of claims 1-18, a fusion protein according to claim 19 or 20, a nucleic acid molecule according to claim 22, an antisense nucleic acid molecule according to claim 23, an activator compound according to claim 28, a modulator compound according to claim 30, or a pharmaceutical composition according to claim 34.~~

37 (Currently amended): The ~~Use according to claim 35 or~~ method according to claim 36 wherein said disease is a neurological disease or cancer.

38 (Currently amended): The ~~Use or~~ method according to claim 37 wherein said disease is leukaemia.

39 (Currently amended): A method of diagnosing a conditions associated with an aberrant activity of a tyrosine kinase protein comprising measuring the level of an aberrant tyrosine kinase protein in a cell sample obtained from a patient using a tyrosine kinase inhibitor protein according to claim 1 ~~any one of claims 1-18~~.

40 (Currently amended): A method of diagnosing a condition associated with an aberrant tyrosine kinase activity of c-Abl protein comprising using a nucleic acid molecule according to claim

22 ~~or an antisense nucleic acid molecule according to claim 23~~ to screen for mutations in the cap region.

41 (Original): A transgenic animal comprising a nucleic acid molecule according to claim 22.

42 (Original): A c-Abl protein comprising a protease cleavage site located near the boundary of the cap region and the SH3 domain.

43 (Original): A c-Abl protein according to claim 42 wherein said protease cleavage site is a TEV protease cleavage site.

44 (Currently amended): A fusion protein comprising a c-Abl protein according to claim 42 ~~or claim 43~~ fused to a marker domain.

45 (Currently amended): A method for activating the tyrosine kinase activity of c-Abl comprising supplying a cell with a c-Abl protein comprising a protease cleavage site according to claim 42 ~~or claim 43 or a fusion protein according to claim 44~~ and supplying the cell with a protease to cleave at the protease cleavage site.

46 (Currently amended): A method for producing an activated c-Abl protein comprising cleaving a c-Abl protein according to claim 42 ~~or claim 43 or a fusion protein according to claim 44~~ with a protease and isolating the cleaved C-terminal region of said c-Abl protein.

47 (Currently amended): A method for producing a tyrosine kinase inhibitor protein comprising cleaving a c-Abl protein according to claim 42 ~~or 43 or a fusion protein according to claim 44~~ with a protease and isolating the cleaved N–terminal cap region of said c-Abl protein.

48 (Currently amended): A nucleic acid molecule encoding a c-Abl protein according to claim 42 ~~or claim 43 or a fusion protein according to claim 44~~.

49 (Original): A method for activating a c-Abl protein comprising introducing a nucleic acid molecule according to claim 48 into a cell under conditions in which it is expressed and supplying said cell with a protease.

50 (Original): A method for producing an activated c-Abl protein comprising introducing a nucleic acid molecule according to claim 48 into a cell under conditions in which it is expressed, supplying said cell with a protease and isolating the cleaved C-terminal region of said c-Abl protein

51 (Original): A method for producing a tyrosine kinase inhibitor protein comprising introducing a nucleic acid molecule according to claim 48 into a cell under conditions in which it is expressed, supplying said cell with a protease and isolating the cleaved N-terminal cap region of said c-Abl protein.

52 (Original): A transgenic animal comprising a nucleic acid molecule according to claim 48.

53 (Original): A method for activating tyrosine kinase activity of c-Abl *in vivo* comprising supplying a transgenic animal according to claim 52 with a protease.

54. (Original): A method for screening for a compound that restores autoinhibition of c-Abl *in vivo* comprising supplying a transgenic animal according to claim 52 with a protease to activate the tyrosine kinase activity of c-Abl, supplying the transgenic animal with a candidate compound and assessing the effect of the candidate compound on the tyrosine kinase activity in the cells of said transgenic animal.

55 (New): An antibody that binds to a fusion protein according to claim 19.

56 (New): A nucleic acid molecule encoding a fusion protein according to claim 19.

57 (New): An antisense nucleic acid which binds under high stringency conditions to a nucleic acid molecule according to claim 56.

58 (New): A vector comprising a nucleic acid molecule according to claim 23.

59 (New): A vector comprising a nucleic acid molecule according to claim 56.

60 (New): A vector comprising a nucleic acid molecule according to claim 57.

61 (New): A host cell transformed or transfected with nucleic acid molecule according to claim 23.

62 (New): A host cell transformed or transfected with nucleic acid molecule according to claim 56.

63 (New): A host cell transformed or transfected with nucleic acid molecule according to claim 57.

64 (New): A host cell transformed or transfected with a vector according to claim 24.

65 (New): A host cell transformed or transfected with a vector according to claim 58.

66 (New): A host cell transformed or transfected with a vector according to claim 59.

67 (New): A host cell transformed or transfected with a vector according to claim 60.

68 (New): A method for preparing a tyrosine kinase inhibitor protein or a functional equivalent thereof comprising culturing a host cell containing a nucleic acid molecule according to claim 56 under conditions whereby said protein is expressed and recovering said protein thus produced.

69 (New): A method of diagnosing a condition associated with an aberrant tyrosine kinase activity of c-Abl protein comprising using a nucleic acid molecule according to claim 22 to screen for mutations in the cap region.

70 (New): A method for activating the tyrosine kinase activity of c-Abl comprising supplying a cell with a c-Abl protein comprising a protease cleavage site according to claim 44 or a fusion protein and supplying the cell with a protease to cleave at the protease cleavage site.

71 (New): A method for producing an activated c-Abl protein comprising cleaving a c-Abl protein according to a fusion protein according to claim 44 with a protease and isolating the cleaved C-terminal region of said c-Abl protein.

72 (New): A method for producing a tyrosine kinase inhibitor protein comprising cleaving a c-Abl protein according to a fusion protein according to claim 44 with a protease and isolating the cleaved N–terminal cap region of said c-Abl protein.

73 (New): A nucleic acid molecule encoding a c-Abl protein or a fusion protein according to claim 44.